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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,844	03/17/2000	Timothy J. Barberich	4821-334-999	3697

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EXAMINER	
BAHAR, MOJDEH	

ART UNIT	PAPER NUMBER
1617	19

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/527,844	Applicant(s) BARBERICH ET AL.	
	Examiner Mojdeh Bahar	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 50-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 50-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response to the office action of November 5, 2002, and amendment submitted April 4, 2003 is acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al. abstract (AN 1997: 593623 CAPLUS).

Davis et al. abstract discloses ziprasidone as an antipsychotic drug having high affinity for serotonin 5-HT2 and dopamine D2 receptors. Davis et al. further discloses that clinical trials have shown ziprasidone to be effective in treating depression associated with schizophrenia, and in reducing anxiety in patients about to undergo dental surgery, see abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 and 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. abstract (AN 1997: 593623 CAPLUS) in view of Lowe et al. (USPN 4,831,031), Allen et al. (USPN 5,312,925) and Parkash et al.

Davis et al. abstract discloses ziprasidone as an antipsychotic drug having high affinity for serotonin 5-HT2 and dopamine D2 receptors. Davis et al. further discloses that clinical trials have shown ziprasidone to be effective in treating depression associated with schizophrenia, and in reducing anxiety in patients about to undergo dental surgery, see abstract.

Davis et al. does not specifically teach metabolites of ziprasidone, amounts (i.e., dosage), routes of administration.

Lowe et al. (USPN 4,831,031) teaches that aryl piperazinyl (C2-C4) alkylene heterocyclic compounds (including ziprasidone) and their pharmaceutically acceptable salts, known neuroleptic agents, can be administered orally, in form of tablets or capsules or parentrally, see col. 3, line 54-col.4 line 33. Lowe et al also teaches that a daily dosage range is from 5 to 500 mg, see in particular col. 4, lines 3-33, see also claims 1-9.

Allen et al. (USPN 5,312,925) specifically teaches the employment of ziprasidone hydrochloride as a neuroleptic agent.

Parkash teaches the affinity of the sulfone and sulfoxide metabolites of ziprasidone for 5-HT2 and D2 receptors.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ ziprasidone or any of its known salts or metabolites in a method of treating neuroleptic disorders.

One of ordinary skill in the art would have been motivated to employ ziprasidone or any of its known salts or metabolites in a method of treating neuroleptic disorders, because ziprasidone in general and ziprasidone hydrochloride are known neuroleptic agents employed in treating anxiety, depression associated with schizophrenia and situational anxiety (i.e., anxiety prior to dental surgery). Employment of different salts and metabolites of a known active is within the skill of the artisan and therefore obvious.

Response to Arguments

Applicant's arguments filed April 4, 2003 have been fully considered but they are not persuasive. In response to the rejection under 35 USC 102, applicant argues that the instant claims are drawn to a method of employing ziprasidone metabolites and not ziprasidone itself in treating disorders ameliorated by the inhibition of seratonin reuptake and/or dopamine reuptake. As set forth in the previous office action, note that ziprasidone converts to its metabolites *in vivo*. Therefore the administration of ziprasidone results in its conversion to metabolites thereof. Consequently, the administration of ziprasidone necessarily and inherently results in its administration/conversion to ziprasidone metabolites *in vivo*. Therefore each and every element of the claim is indeed met. Applicant then argues that the disclosure of dosage forms in the specification presupposes the existence of a ziprasidone metabolite prior to its administration to a patient. Note that none of the claims rejected under 35 USC 102 recites a dosage form and arguments as to unclaimed limitations are moot. In response to applicant's argument that the

references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., inclusion of the metabolites in the dosage forms) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant then argues that there is no motivation to combine the three prior art references used in the obviousness rejection. Applicant argues that none of the three references teaches the employment of ziprasidone metabolites. Note that all references teach the employment of ziprasidone itself and as argued herein above, the employment of the metabolites of ziprasidone would result in the same *in vivo* activity. Therefore following the court's ruling in *Zenith Laboratories Inc. v. Bristol-Myers Squibb Co.*, the Skilled Artisan would know that the compound Ziprasidone is not limited to "its pre-ingested form", 30 USPQ2d 1285, 1289. In the instant case the ziprasidone metabolites are employed to treat disorders ameliorated by the inhibition of seratonin reuptake and/or dopamine reuptake. Ziprasidone itself is known to be useful in treating these diseases via the same mechanisms, therefore it would have been obvious to employ the metabolites in lieu of ziprasidone in treating these same disorders. Applicant further argue and supply the Ereshefsky reference showing that the ziprasidone metabolites are inactive. Note the Parkash et al. reference in the 103 rejection herein above which teaches that ziprasidone sulfone and sulfoxide--though not as active as ziprasidone itself--nevertheless exhibit affinities for 5-HT2 and D2 receptors. Therefore at the very least the particular metabolites taught in Parkash et al. are not inactive.

Applicant then argues against the obviousness rejection, stating that in order for administration of ziprasidone metabolites to result in the same *in vivo* activity as the administration of ziprasidone itself, ziprasidone itself must be inactive. As shown herein above in the Parkash et al. reference, both ziprasidone and its metabolites are known to have affinities for 5-HT2 and D2 receptors, therefore they have the same activity.

Applicant finally argues that Examiner's reliance on Zenith is misplaced. It appears that the applicant argues that the court's reasoning cannot be applicable to the case at bar because Zenith was an infringement case and did not concern anticipation or obviousness. Note that although the case was based on an infringement suit, the court's reasoning is nevertheless applicable to the case at bar since one of the questions before the court was the relation between pre-ingested and ingested form of a drug.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703) 305-1877. The fax number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
June 10, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER
6/14/03